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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,160	03/01/2007	Mary Ellen Rybak	13566.105023	1564
65989	7590	03/20/2008		
KING & SPALDING 1185 AVENUE OF THE AMERICAS NEW YORK, NY 10036-4003			EXAMINER LEWIS, PATRICK T	
			ART UNIT 1623	PAPER NUMBER
			NOTIFICATION DATE 03/20/2008	DELIVERY MODE ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/579,160	<b>Applicant(s)</b> RYBAK, MARY ELLEN	
	<b>Examiner</b> Patrick T. Lewis	<b>Art Unit</b> 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3-18 and 21-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-18 and 21-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02042008</u>  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Applicant's Response Dated February 4, 2008***

1. Claims 1, 3-18 and 21-25 are pending. An action on the merits of claims 1, 3-18 and 21-25 is contained herein below.
2. The objection to claims 17-20 has been rendered moot in view of applicant's amendment dated February 4, 2008.
3. The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Bowman et al. WO 00/69441 (Bowman) has been rendered moot in view of applicant's amendment dated February 4, 2008.
4. The rejection of claims 1, 3-16 and 21 under 35 U.S.C. 103(a) as being unpatentable over Bowman et al. WO 00/69441 (Bowman) in combination with Ishikawa et al. Biochemical Pharmacology (1998), Vol. 55, pages 1091-1097 (Ishikawa) is maintained for the reasons of record as set forth in the Office action mailed on November 2, 2007. Newly amended claims 17-18 and newly added claims 22-25 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Bowman et al. WO 00/69441 (Bowman) in combination with Ishikawa et al. Biochemical Pharmacology (1998), Vol. 55, pages 1091-1097 (Ishikawa) as applied to claims 1, 3-16 and 21 in the Office action mailed on November 2, 2007.

***Rejections of Record Set Forth in the Office Action Dated November 2, 2007***

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 1, 3-18 and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bowman et al. WO 00/69441 (Bowman) in combination with Ishikawa et al. Biochemical Pharmacology (1998), Vol. 55, pages 1091-1097 (Ishikawa).

Claims 1, 3-18 and 22-25 are drawn to a method of treating a human body having cancer comprising administering an effective therapeutic amount of ET-743 in combination with an effective therapeutic amount of a 5-fluorouracil pro-drug thereof. Claim 21 is drawn to a medical kit for administering ET-743 in combination with capecitabine.

Bowman teaches treating any mammal affected by cancer comprising administering a therapeutically effective amount of ET-743, or a pharmaceutical composition thereof (pages 7-8). Administration of the compounds is preferably by intravenous infusion. Infusion times of up to 72 hours are used. The correct dosage of the compound will vary according to the particular formulation, mode of application, and the particular *situs*, host and tumor being treated. Administration can be carried out continuously or periodically within the maximum tolerated dose. ET-743 may be used with other drugs to provide a combination therapy. The other drugs may form part of the same composition, or be provided as a separate composition for administration at the same time or a different time. Suitable candidates include antimetabolite drugs such as 5-fluorouracil.

Bowman differs from the instantly claimed invention in that Bowman does not teach the administration of capecitabine or other 5-fluorouracil pro-drugs; however, the use of capecitabine would have been obvious to one of ordinary skill in the art at the time of the invention.

Ishikawa teaches that cytotoxic anticancer drugs often cause severe side-effects because they do not act selectively in tumors. Capecitabine was designed to generate the active drug 5-FUra selectively in human tumors through three sequential steps of enzyme reactions in humans. Because these enzymes are so localized in the body, capecitabine is expected to generate 5-Fura selectively in tumor tissues, and consequently, to improve the efficacy and safety margins of 5-FUra, the parent drug.

It would have been obvious to one of ordinary skill in the art to use capecitabine. As taught by Ishikawa, capecitabine generates the active drug 5-FUra selectively and consequently, improves the efficacy and safety margins of the parent drug. Selection of appropriate dosage regimens will vary according to the particular formulation, mode of application, and the particular *situs*, host and tumor being treated, and such selection would have been well within the purview of the skilled artisan.

7. Applicant's arguments filed February 4, 2008 have been fully considered but they are not persuasive. Applicant argues that 1) the references fail to teach all of the claimed elements, and 2) the references fail to provide a reason for one of ordinary skill in the art to arrive at the claimed elements.

Applicant's arguments are not persuasive. There is clearly motivation to combine the references cited in the instant rejection. Use of materials in combination, each of

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which is known to function for intended purpose, is generally held to be prima facie obvious as the idea of combining them flows logically from their having been individually taught in the prior art. In the instant case, Bowman teaches treating any mammal affected by cancer comprising administering a therapeutically effective amount of ET-743, or a pharmaceutical composition thereof (pages 7-8). Ishikawa teaches the use of capecitabine for the treatment of cancer. Thus, claims that require no more than the administration of two conventional anti-cancer compositions together in order to treat cancer in a patient set forth prima facie obvious subject matter. Furthermore, Bowman clearly suggests using ET743 in combination with other drugs for cancer treatment. See page 8 of Bowman.

Takahashi et al. and applicant's contention that the prior art teaches away from the instant invention have been noted; however, Ishikawa explicitly teaches the preference for using capecitabine over 5-fluorouracil and provides possible explanations for its superiority. Ishikawa teaches, "we concluded that capecitabine should be much safer and more effective than 5-FUra. In fact, capecitabine was much more effective at a wider dose range than 5-FUra in the human colon cancer xenograft models used in the present study." Selection of appropriate dosage regimens will vary according to the particular formulation, mode of application, and the particular *situs*, host and tumor being treated, and such selection would have been well within the purview of the skilled artisan.

### ***Conclusion***

8. Claims 1, 3-18 and 21-25 are pending. Claims 1, 3-18 and 21-25 are rejected. No claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### ***Contacts***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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/Dr. Patrick T. Lewis/  
Primary Examiner, Art Unit 1623

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